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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/988,966	11/19/2001	Bjorn M. Nilsson	13425-055001	9672

26161 7590 01/08/2003

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EXAMINER	
BERNHARDT, EMILY B	
ART UNIT	**PAPER NUMBER**
1624	9

DATE MAILED: 01/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/988,966	NILSSON et al.
Examiner	**Art Unit**
Emily Bernhardt	1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-24 is/are pending in the application.

4a) Of the above, claim(s) 18-24 is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1-17 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 5
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-17, drawn to compounds,compositions and uses where R3/R4 do not fuse, classified in class 544, subclasses such as 357 and others as determined by the nature of substituents thereon; class 514 subclasses such as 252.11,235.8.

II. Claims 1-5,7-10,12-17, drawn to compounds,compositions and uses where pyrazine ring is fused at R3/R4, classified in class 544, subclasses such as 354 (for quinoxalines), 350 (for thienofused compounds),etc.;class 514 subclasses such as 248,249,etc.

III. Claims 18-24, drawn to a process for making compounds of I, classified in class 544, subclass 357,etc.

IV. Claims 18-24, drawn to a process for making compounds of II, classified in class 544, subclasses 350,354,etc.

If II or IV elected applicants must further elect a specific pyrazine core.

The inventions are distinct, each from the other because of the following reasons: Compounds of I and II are drawn to differing cores which are consequently

separately classified, and would be expected to raise different issues of patentability in view of the structural dissimilarity for compounds of I vs II as a whole. Each can support a patent as the compounds of each group are capable of being utilized alone not in combination with other members listed in the Markush group.

Inventions I-II and III-IV are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case more than one type of pyrazine reactant and alcohol reactant can be employed to make instant products as suggested by Nilsson (WO'984) in method C.

During a telephone conversation with Dr. Hsi on 12/18/02 a provisional election was made with traverse to prosecute the invention of I, claims 1-17. Affirmation of this election must be made by applicant in replying to this Office action. Claims 18-24 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claims which link inventions I and II will only be examined with respect to the elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claims 1-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. "Protecting groups" in main claim 1 requires clarification since the claims appear to be directed to final products (note method claims depend on claim 1) yet from a reading of the specification said groups are only being used as synthetic precursors for one step. Even if the purpose of such was only for protection in synthetic procedures, it is not clear what other goups are contemplated other than the 3

described on on p.9 or 11 of the specification . There is no such thing as a universal protecting group.

2."Aryl" is not clearly defined in the specification . Note the wording "includes" on p.8 which is open to the inclusion of other rings. The same applies to the term "heteroaryl" on p.8 . Wording in the specification should be modified to "means" from "includes" to make intent clear.

3. Nature of intended rings formed at NR5R6 is not adequately set forth. The only atom identified as a ring member is the N. Note In re Wiggins 179 USPQ 421 regarding such terminology.

4. The scope of "prodrug forms" is completely unknown. More than minimal experimentation would be required to determine what is and what is not within the instant scope since the choice of a suitable prodrug requires testing for rate of hydrolysis as well as in vivo stability and knowledge of an intended effect (i.e. modification of a undesirable property in the parent drug) and such is a function of the molecular structure of the parent drug as any textbook on prodrugs will confirm. Specification provides no guidance.

5.Claim 11 recites subject matter outside the scope of main claim 1. The former recites "solvates" while the latter recites "hydrates". The two terms are not synonymous. Other than hydrates specification provides no guidance as to other solvents being suitable as solvates.

6. Method claims 13,14 and 17 are of indeterminate scope for the following reasons. No one particular disorder is recited. The claim language may read on diseases not yet known to be affected by serotonin receptors in general as recited in claim 13 or 5HT2c in particular as recited in claim 14. Also,how does one determine who is in need and who is not? No criteria is described. To what other serotonin receptors are instant compounds capable of binding? What's the difference in scope for claims 14 vs 17? What interaction qualifies as "modulating"? Additionally, determining whether a given disease responds or not to serotonin binding involves much experimentation since a negative response from one patient does not mean the drug isnt useful as no drug has 100% effectiveness. Thus what "success rate" determines if a particular inhibitor is effective and how many patients (and dosage regimens) need to be tested? The test for determining compliance with 35 USC 112, par.two

is whether applicants have clearly defined "their" invention not what may be discovered by future research as this type of claim language clearly requires.

Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. .

1.Specification is not adequately enabled for the scope of pyrazines claimed which can have a plethora of functional groups containing heteroaryls at various locations as well as a nonlimiting array of saturated NR5R6-containing rings and any and all N-protected derivatives thereof. Only 5 compounds have been prepared and out of these, only 2 tested for only 5HT2c receptor binding activity. Receptor binding is known to be structure-sensitive as evidenced at the very least by applicants' own statement made in the specification (on p.19) that for exemplary compounds of the invention the range in activity varied as much as 1500-fold. Note In re Surrey 151 USPQ 724 regarding sufficiency of disclosure for a Markush group. Also see MPEP 2164.03 for enablement requirements in cases directed to structure-sensitive arts such as the pharmaceutical art. Also note the criteria for enablement as set out in In

re Wands cited in MPEP 2164.01(a),August 2000 edition. Thus given the breadth of the claims, the level of unpredictability in the art and the lack of direction (i.e. working examples) provided as to what other rings,ring systems as heteroaryl (at various locations) and NR5R6 rings (other than those recited in claim 9) might work, this rejection is being applied.

2.Scope of solvates in dependent claim 11 is not enabled since generally not all solvents can form solvates with all compounds. There is no process enabling such a scope in the specification .

3. Applicants provide no reasonable assurance that any and all "prodrug" derivatives of instant compounds will have the ability to generate the instant compounds in vivo by one or more processes. Additionally method claims include such moieties. Generally, prodrugs themselves are not considered to be therapeutically active but only to provide the active compound in vivo.

4. Applicants provide no definitive evidence to correlate the many disease states being claimed which from a reading of the specification includes all cognitive disorders, all forms of sexual dysfunction, eating disorders,etc. as treatable based on the ability of instant compounds to bind to the 5HT2c receptor. While treating

anxiety,depression has been strongly linked to 5HT2c antagonism (see Gaster especially page 26,provided with this action), uses such as sexual dysfunction have not nor have all cognitive and eating disorders. Thus, Gaster at the very least evidences that the level of skill in the art is not so high as to warrant treatment of all diseases positively recited in the specification and embraced by the current claim language.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nilsson (WO'984). The comonly assigned publication discloses similar compounds to that claimed herein and for the same uses based on 5HT2c receptor binding. See formula (I) and definition of all variables therein especially substituents on R listed on p.5. While example 77 does not anticipate the instant scope it only differs in having the morpholine ring directly attached to the phenyl vs instant methylene as a link between said two rings. Note that Nilsson teaches not only saturated heteros

directly attached to phenyl (as "R" in the WO) but also indirect attachment with C1-C6 alkylene as described on p.5, line 17. Thus it would have been obvious to one skilled in the art at the time the invention was made to replace morpholino with morpholinomethyl and obtain an additional compound having the uses urged by Nillson in view of the equivalency teaching outlined above.

It is recognized applicants are urging benefit under 35 USC 119. However benefit is not being granted for the following reasons. For benefit there must be clear compliance with 35 USC 112, description and enablement as was decided in In re Gostelli 10 USPQ 2nd 1614; Kawai v. Metlesics 178 USPQ 158. At the very least instant claims do not comply with 35 USC 112 par.one for reasons given in the above 112 rejection and additionally are of broader scope than that described in said priority ~~paper~~ papers. Note the absence of nitrogen protecting groups as well as solvates covered by claim 1 and 11, respectively.

Claims 1-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nillson (US'467). Should applicants be ultimately entitled to 119 benefit, the US equivalent to WO''467 would still be a competent reference as its filing date antedates applicants' foreign priority date. It otherwise has the same disclosure as

the WO publication and is applied for the same reason as the WO as discussed in the above 103 rejection.While evidence of common ownership may now be enough to disqualify commonly assigned art under 103 based on 102(e) as well as 102(f) or (g) in view of the passage of the American Inventors Protection Act, there must be provided a clear statement by applicants, attorney or agent of record that instant application and US Nilsson **at the time the instant invention was made** were commonly owned. See 1241 OG 96, December 26,2000.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory

double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-17 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of U.S. Patent No. 6465467. Although the conflicting claims are not identical, they are not patentably distinct from each other because they embrace overlapping subject matter. Note formula Ib in the patent claims cover instant subject matter when NR5R6 is a ring such as morpholino, and others described in col.6 of the US patent. See substituent "heterocycl C1-6 alkyl" covered by the patent claims.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302).

Commonly assigned 6,465,467, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case

qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 37 CFR 1.78(c) and 35 U.S.C. 132 to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

Any inquiry concerning this communication should be directed to Emily Bernhardt at telephone number (703) 308-4714.

A facsimile center has been established for Group 1600. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier

numbers for accessing the facsimile machine are (703) 308-4556 or (703) 305-3592.

E Bernhardt

EMILY BERNHARDT

PRIMARY EXAMINER

GROUP 1600